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Applicant	:	Bernhard GLEICH
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Title: METHOD AND APPARATUS FOR IMPROVED DETERMINATION OF SPATIAL NON-AGGLOMERATED MAGNETIC PARTICLE DISTRIBUTION IN AN AREA OF EXAMINATION

APPEAL BRIEF

Mail Stop **Appeal Brief - Patents**
Commissioner for Patents
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Sir:

In response to the FINAL Office Action dated 21 October 2010, and in support of the Notice of Appeal filed on 11 January 2011, Applicant hereby respectfully submits this Appeal Brief.

REAL PARTY IN INTEREST

Koninklijke Philips Electronics N.V. owns all of the rights in the above-identified U.S. patent application.

RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences related to this application or to any related application, nor will the disposition of this case affect, or be affected by, any

other application directly or indirectly.

STATUS OF CLAIMS

Claims 1, 19 and 23-24 are canceled.

Claims 2-18, 20-22 and 25 are pending in the application.

Claims 2-18, 20-22 and 25 all stand rejected.

Accordingly, the claims on appeal are claims 2-18, 20-22 and 25.

STATUS OF AMENDMENTS

There are no pending amendments with respect to this application.

SUMMARY OF CLAIMED SUBJECT MATTER

The present invention is directed to a method of ultrasound molecular imaging of tissue using contrast agents.[1]

Accordingly, as broadly recited in claim 2, a method (FIG. 1) is provided to determine the spatial distribution of magnetic particles in an examination area of an object. The method comprises: a) (FIG. 1 – first step; page 13, lines 25-29) generating a first magnetic field having a field strength with a spatial distribution such that the first magnetic field has a lower magnetic field strength in a first sub-area of the examination area and the first magnetic field has a higher magnetic field strength in a second sub-area of the examination area, and wherein a gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area (page 6, lines 19-22); b) (FIG. 1 – second step; page 13, lines 30-31) changing the spatial location of both the first and second sub-areas in the examination area, including changing a location where the gradient of the first magnetic field reverses

1 In the description to follow, citations to various reference numerals, figures, and corresponding text in the specification are provided solely to comply with Patent Office rules. It should be understood that these reference numerals, figures, and text are exemplary in nature, and not in any way limiting of the true scope of the claims. It would therefore be improper to import anything into any of the claims simply on the basis of **exemplary** language that is provided here only under the obligation to satisfy Patent Office rules for maintaining an Appeal.

direction and experiences a zero crossing within the first sub-area, so that a magnetization of the magnetic particles changes locally (page 6, line 30 – page 7, line 5); c) (FIG. 1 – third step; page 14, lines 1-2; page 7, lines 8-13) acquiring signals that depend on the magnetization of the magnetic particles in the examination area influenced by the changed spatial locations of both the first and second sub-areas in the examination area; and d) (FIG. 1 – third step; page 14, lines 3-4) evaluating said signals to determine the spatial distribution of the magnetic particles in the examination area, wherein before or during the determining of the spatial distribution of the magnetic particles in the examination area the magnetic particles are exposed to a second, time-varying, magnetic field so as at least to reduce agglomeration of the magnetic particles (page 14, lines 5-7).

As broadly recited in claim 22, an apparatus (FIG. 2 – element 200) is provided to determine the spatial distribution of magnetic particles in an area of examination of an object. The apparatus comprises: a) means (FIG. 2 – element 210; page 13, lines 25-29) for generating a first magnetic field with a spatial distribution such that the first magnetic field has a lower magnetic field strength in a first sub-area (FIG. 2 – element 12) of the examination area (FIG. 2 – element 10) and the first magnetic field has a higher magnetic field strength in a second sub-area (FIG. 2 – element 14) of the examination area, and wherein a gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area (page 6, lines 19-22); b) means (FIG. 2 – element 220; page 13, lines 30-31) for changing the spatial location of both the first and second sub-areas in the area of examination, including changing a location where the gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area, so that a magnetization of the magnetic particles changes locally (page 6, line 30 – page 7, line 5); c) means (FIG. 2 – element 230; page 14, lines 1-2; page 7, lines 8-13) for acquiring signals that depend on the magnetization of the magnetic particles in the area of examination influenced by the changed spatial locations of both the first and second sub-areas in the examination area; and d) means for evaluating (FIG. 2 – element 240; page 14, lines 3-4) the signals to determine a spatial distribution of the magnetic particles in the area of examination, wherein the means for changing the

spatial location of both the first and second sub-areas in the area of examination include means (FIG. 2 – element 220; page 14, lines 5-7) for imposing in at least part of the first sub-area a second, time-varying, magnetic field.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The grounds of rejection to be reviewed on Appeal are: (1) the rejections of claims 2-9, 11-13, 16-18, 22 and 25 under 35 U.S.C. § 103 over Tournier et al. U.S. Patent Application Publication 2002/0168321 ("Tournier") in view of Kreuwel et al. U.S. Patent 6,764,859 ("Kreuwel"); (2) the rejections of claims 10, 14, 15 and 20 under 35 U.S.C. § 103 over Tournier in view of Kreuwel and further in view of Ivkov U.S. Patent Application Publication 2006/0142749 ("Ivkov"); and (3) the rejection of claim 21 under 35 U.S.C. § 103 over Tournier in view of Kreuwel and further in view of Rand U.S. Patent Application Publication 2005/0066961 ("Rand").

ARGUMENTS

(1) Claims 2-9, 11-13, 16-18, 22 and 25 Are Patentable Under 35 U.S.C. § 103 Over Tournier & Kreuwel

At the outset, Applicant relies on at least on the following standards with regard to proper rejections under 35 U.S.C. § 103. First, a rejection on obviousness grounds under 35 U.S.C. § 103 cannot be sustained by mere conclusory statements: instead there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). See also KSR International Co. v. Teleflex Inc., 550 U.S. 398, 82 USPQ2d 1385, 1396 (2007) (quoting Federal Circuit statement with approval) See M.P.E.P. § 2141(III). Second, there must be a reasonable expectation of success. "*The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art.*" M.P.E.P. § 2143.01(III) (citing KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385, 1396 (2007)). Finally, the prior art reference (or references when combined) must teach or suggest all the claim

limitations. "*All words in a claim must be considered in judging the patentability of that claim against the prior art*." M.P.E.P. § 2143.03 (citing In re Wilson, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970)). An integral part of this analysis requires establishing the level of ordinary skill in the art of invention of claim 1. See M.P.E.P. §§ 2141(II)(C) and 2141.03.

Claim 22

Applicant respectfully traverses the proposed modification of Tournier's device in the rejection of claim 22 under 35 U.S.C. § 103 for at least the reason that the proposed combination of teachings lacks an articulated reasoning with some rational underpinning.

Among other things, the apparatus of claim 22 includes means for generating a first magnetic field with a spatial distribution such that the first magnetic field has a lower magnetic field strength in a first sub-area of the examination area and the first magnetic field has a higher magnetic field strength in a second sub-area with a higher magnetic field strength of the examination area, and wherein a gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area, and means for changing the spatial location of both the first and second sub-areas in the area of examination, including changing a location where the gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area, so that a magnetization of the magnetic particles changes locally.

The Examiner fairly admits that Tournier does not teach means for changing the spatial location of first and second sub-areas where the first (imaging) magnetic field has the higher and lower field strengths, or that a gradient of the first (imaging) magnetic field reverses direction and experiences a zero crossing within the first sub-area, or means for changing the location where the gradient of the first magnetic field reverses direction and experiences a zero crossing.

The Examiner insists that Kreuwel teaches these features and that it would have been obvious to have modified Tournier to include these features "*in order to prevent agglomeration of the magnetic particles*."

Applicant respectfully disagrees.

At the outset. the Examiner fails to explain where the combination of Tournier and Kreuwel provide a teaching that one should "*chang*[e] *the spatial location of both the first and second sub-areas in the area of examination, including changing a location where the gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area*" as recited in claim 22. The Examiner cites nothing in either Tournier or Kreuwel that discloses such a combination of features. Indeed, the Examiner fails to even mention "*changing the spatial location of both the first and second sub-areas in the area of examination, including changing a location where the gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area*" as recited in claim 22.

So no combination of Tournier and Kreuwel could ever produce the apparatus of claim 22.

The Examiner also argues that Kreuwel teaches subjection of magnetic particles to a varying magnetic field, "*wherein the field is reversed (i.e., oscillated, such that the relative position of the examination area changes relative to the magnetic field)*."

Applicant respectfully disagrees.

Kreuwel does not pertain to any imaging magnetic fields, but instead is concerned with mixing magnetic particles in a fluid by subjecting them to a magnetic field with different and changing directions. Kreuwel does not disclose or pertain to any "examination area." Therefore it is not possible for Kreuwel to teach "*the relative position of the examination area changes relative to the magnetic field*" as asserted by the Examiner.

So, again, no combination of Tournier and Kreuwel could ever produce the apparatus of claim 22.

Applicant also traverses the proposed modification of Tournier to add the means for changing the spatial location of first and second sub-areas where the first (imaging) magnetic field has the higher and lower field strengths, and to add the feature that a gradient of the first (imaging) magnetic field reverses direction and

experiences a zero crossing within the first sub-area, and to add the means for changing the location where the gradient of the first magnetic field reverses direction and experiences a zero crossing. Applicant respectfully submits that the proposed modification lacks any reason with rational underpinnings based on the demonstrated knowledge and teachings available to one of ordinary art at the time of the invention.

The Examiner appears to be arguing that the combination of Kreuwel's teaching with Tournier's would not only have produced an apparatus which added the time-varying field of claim 22 to Tournier's imaging magnetic field "*in order to prevent agglomeration of the magnetic particles*:" but would have **also** modified Tournier's imaging magnetic field – for reasons unknown – to vary the spatial location of the first and second sub-areas where the first (imaging) magnetic field has the higher and lower field strengths, and would have **also** modified Tournier's imaging magnetic field to provide that a gradient of the first (imaging) magnetic field reverses direction and experiences a zero crossing within the first sub-area, and would have **also** modified Tournier's imaging magnetic field to change a location where a gradient of the first magnetic field reverses direction and experiences a zero crossing (which reversal of direction and zero-crossing are not even present in Tournier's magnetic field).

At this point, it is important to carefully note that claim 1 does **not** recite that the second (time-varying) magnetic field has the first and second sub-areas where the first (time-varying) magnetic field has the higher and lower field strengths and the spatial locations of these first and second sub-areas are varied. Nor does claim 1 recite that a gradient of the second (time-varying) magnetic field reverses direction and experiences a zero crossing within the first sub-area. Nor does claim 1 recite that a location where a gradient of the second (time-varying) magnetic field reverses direction and experiences a zero crossing is changed.

Instead, these features in claim 22 are clearly recited as pertaining to the **first** (imaging) magnetic field – the magnetic field for which the Examiner cites Tournier, not the second (time-varying) magnetic field for which the Examiner cites Kreuwel.

It is unknown on what basis the Examiner asserts that one of ordinary skill in the art upon reading Kreuwel's disclosure would have come to the conclusion that

she/he should modify Tournier's imaging magnetic field (supposedly corresponding to the first magnetic field of claim 22) to vary the spatial location of the first and second sub-areas where the first (imaging) magnetic field has the higher and lower field strengths, and also that she/he should modify Tournier's imaging magnetic field such that a gradient of the first (imaging) magnetic field reverses direction and experiences a zero crossing within the first sub-area.

At most, one of ordinary skill in the art upon reading Kreuwel's disclosure might have come to the conclusion that she/he should modify Tournier's arrangement to add a second time-varying magnetic field to prevent agglomeration. And assuming *arguendo* that Kreuwel "inherently" teaches that his time-varying magnetic field has an area where the gradient of the time-varying magnetic field experiences a zero crossing, then one of ordinary skill in the art upon reading Kreuwel's disclosure might have come to the conclusion that she/he should modify Tournier's arrangement to add a second time-varying magnetic field where that **second time-varying magnetic field** includes an area where the gradient of the time-varying magnetic field experiences a zero crossing.

However that is not what is recited in claim 22. Claim 22 recites that it is the gradient of the **first magnetic field** (i.e., **the imaging magnetic field for which the Examiner cites Tournier**, and not the second, time-varying magnetic field for which the Examiner cites Kreuwel) which reverses direction and experiences a zero crossing within the first sub-area.

Furthermore, there is nothing in Kreuwel that teaches that Tournier's imaging magnetic field should be modified to vary the spatial location of the first and second sub-areas where the first (imaging) magnetic field has the higher and lower field strengths, or that Tournier's imaging magnetic field should be modified to change a location where a gradient of the first magnetic field reverses direction and experiences a zero crossing (which reversal of direction and zero-crossing are not even present in Tournier's magnetic field to be varied!).

Nor has the Examiner explained how or why it is believed that one of ordinary skill in the art at the time of the invention would have had any reasonable expectation

that the Examiner's proposed modification of Tournier (a modification which, again, is not even suggested by the teachings of Tournier and Kreuwel) would produce an apparatus that would (or even could) produce good magnetic imaging results. See M.P.E.P. § 2143.02.

Applicant respectfully submits that such a modification of Tournier can only be based on an impermissible hindsight reconstruction from Applicant's own teachings, and not from what anyone of ordinary skill in the art would have concluded based upon a combination of the teachings of Tournier and Kreuwel.

Therefore, for at least these reasons, Applicant respectfully submits that claim 22 is patentable over the cited prior art. Accordingly, Applicant respectfully requests that the Board reverse the rejection of claim 22.

Claim 2

Among other things, the method of claim 2 includes generating a first magnetic field having a field strength with a spatial distribution such that the first magnetic field has a lower magnetic field strength in a first sub-area of the examination area and the first magnetic field has a higher magnetic field strength in a second sub-area of the examination area, and wherein a gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area, and changing the spatial location of both the first and second sub-areas in the examination area, including changing a location where the gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area, so that a magnetization of the magnetic particles changes locally, wherein before or during the determining of the spatial distribution of the magnetic particles in the examination area the magnetic particles are exposed to a second, time-varying, magnetic field so as at least to reduce agglomeration of the magnetic particles

For similar reasons to those set forth above with respect to claim 22, Applicant respectfully submits that Tournier and Kreuwel, taken individually or collectively, does not disclose or suggest any method having this combination of features.

Therefore, for at least these reasons, Applicant respectfully submits that claim 2 is patentable over the cited prior art. Accordingly, Applicant respectfully requests that the Board reverse the rejection of claim 2.

Claims 3-9, 11-13, 16-18 and 25

Claims 3-9, 11-13, 16-18 and 25 all depend from claim 2 and are deemed patentable over the cited art for at least the reasons set forth above with respect to claim 2. Accordingly, Applicant respectfully requests that the Board reverse the rejections of claims 3-9, 11-13, 16-18 and 25.

(2) Claims 10, 14, 15 and 20 Are Patentable
Under 35 U.S.C. § 103 Over Tournier, Kreuwel & Irkov

Claims 10, 14, 15 and 20 all depend from claim 2.

Applicant respectfully submits that Ivkov does not remedy the deficiencies of Tournier and Kreuwel as set forth above with respect 2.

Therefore, for at least these reasons, Applicant respectfully submits that claims 10, 14, 15 and 20 are patentable over the cited art. Accordingly, Applicant respectfully requests that the Board reverse the rejections of claims 10, 14, 15 and 20.

(3) Claim 21 Is Patentable
Under 35 U.S.C. § 103 Over Tournier, Kreuwel & Rand

Claim 21 depends from claim 2.

Applicant respectfully submits that Rand does not remedy the deficiencies of Tournier and Kreuwel as set forth above with respect 2.

Therefore, for at least these reasons, Applicant respectfully submits that claim 21 is patentable over the cited art. Accordingly, Applicant respectfully requests that the Board reverse the rejection of claim 21.

For all of the foregoing reasons, Applicant respectfully submits that the rejections of claims 2-18, 20-22 and 25 are all in error. Therefore, Applicant respectfully requests that that the Board reverse the rejections of claims 2-18, 20-22

and 25, and the application be returned to the Examiner for further processing.

Respectfully submitted,

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CLAIMS APPENDIX

2. (Previously Presented) A method to determine the spatial distribution of magnetic particles in an examination area of an object, comprising:

a) generating a first magnetic field having a field strength with a spatial distribution such that the first magnetic field has a lower magnetic field strength in a first sub-area of the examination area and the first magnetic field has a higher magnetic field strength in a second sub-area of the examination area, and wherein a gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area,

b) changing the spatial location of both the first and second sub-areas in the examination area, including changing a location where the gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area, so that a magnetization of the magnetic particles changes locally,

c) acquiring signals that depend on the magnetization of the magnetic particles in the examination area influenced by the changed spatial locations of both the first and second sub-areas in the examination area, and

d) evaluating said signals to determine the spatial distribution of the magnetic particles in the examination area, wherein before or during the determining of the spatial distribution of the magnetic particles in the examination area the magnetic particles are exposed to a second, time-varying, magnetic field so as at least to reduce agglomeration of the magnetic particles.

3. (Previously Presented) The method of claim 2, wherein the second magnetic field is superimposed on the first magnetic field at least some of the time.

4. (Previously Presented)The method of claim 2, wherein a strength of the second magnetic field is sufficient to cancel out attractive forces resulting in the agglomeration of the magnetic particles in the examination area.

5. (Previously Presented) The method of claim 2, wherein the second

magnetic field varies in time in all three spatial dimensions.

6. (Previously Presented) The method of claim 25, wherein the particles have an average size or expansion of at least 30 nm.

7. (Previously Presented) The method of claim 2, wherein the second magnetic field is applied in a locally restricted portion of the examination area until the agglomeration of the magnetic particles in at least the locally restricted portion of the examination area is reduced.

8. (Previously Presented) The method of claim 2, wherein the second magnetic field has a frequency in a range of approximately 10 to 500 kHz.

9. (Previously Presented) The method of claim 2, wherein the field strength of the second magnetic field is at least two times greater than the field strength of the first magnetic field.

10. (Previously Presented) The method of claim 2, wherein the magnetic particles are monodomain particles and wherein the field strength of the second magnetic field is at least 30 mTesla.

11. (Previously Presented) The method of claim 25, wherein the magnetic particles comprise a nonmagnetic core covered with a magnetic coating and wherein the field strength of the second magnetic field is at least five mTesla.

12. (Previously Presented) The method of claim 2, wherein the second magnetic field has a power of at least 500 W and is applied in intermittent pulses such that the average power input is less than 500 W.

13. (Previously Presented) The method of claim 2, wherein the second magnetic field is applied as one or more pulses having an amplitude that decays to

zero.

14. (Previously Presented) The method of claim 2, wherein the magnetic particles are in a liquid medium in the examination area and a frequency of the second magnetic field is chosen in view of a viscosity of said liquid medium.

15. (Previously Presented) The method of claim 14, wherein the medium surrounding the magnetic particles is blood and a frequency of the second magnetic field is between 0.7 and 1.3 MHz.

16. (Previously Presented) The method of claim 2, further comprising administering the magnetic particles to the examination area, wherein the second magnetic field is applied to the magnetic particles before administering the magnetic particles to the examination area.

17. (Previously Presented) The method of claim 2, further comprising administering the magnetic particles to the examination area, wherein the magnetic particles are administered to the examination area in an agglomerated state and wherein the magnetic particles in only a part of the examination area are de-agglomerated by exposing only said part of the examination area to the second magnetic field.

18. (Previously Presented) The method of claim 2, wherein a frequency of the second magnetic field is between 0.8 to 1.2 times a frequency of the first magnetic field and wherein the second magnetic field and the first magnetic field are alternately applied to the examination area.

20. (Previously Presented) The method of claim 25, wherein at least one of the magnetic particles is a multi or mono-domain particle that is capable of being reverse magnetized by at least one of Neel rotation and Brownian rotation.

21. (Previously Presented) The method of claim 25, wherein at least one of the magnetic particles is a hard or soft magnetic multi-domain particle.

22. (Previously Presented) An apparatus to determine the spatial distribution of magnetic particles in an area of examination of an object, the apparatus comprising:

a) means for generating a first magnetic field with a spatial distribution such that the first magnetic field has a lower magnetic field strength in a first sub-area of the examination area and the first magnetic field has a higher magnetic field strength in a second sub-area with a higher magnetic field strength of the examination area, and wherein a gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area,

b) means for changing the spatial location of both the first and second sub-areas in the area of examination, including changing a location where the gradient of the first magnetic field reverses direction and experiences a zero crossing within the first sub-area, so that a magnetization of the magnetic particles changes locally,

c) means for acquiring signals that depend on the magnetization of the magnetic particles in the area of examination influenced by the changed spatial locations of both the first and second sub-areas in the examination area,

d) means for evaluating the signals to determine a spatial distribution of the magnetic particles in the area of examination,

wherein the means for changing the spatial location of both the first and second sub-areas in the area of examination include means for imposing in at least part of the first sub-area a second, time-varying, magnetic field.

25. (Previously Presented) The method of claim 2 further including introducing the magnetic particles into the area of examination.

EVIDENCE APPENDIX

{None}

RELATED PROCEEEDINGS APPENDIX

{None}